Applicant: Yoshida et al. Attorney's Docket No.: 20214-0002US1

Serial No.: 10/561,298 Filed: June 7, 2006 Page: 2 of 7

rage : 2 01 /

Amendments to the Claims

This listing of claims replaces all prior versions and listings of claims in the application.

Listing of Claims

1. (Original) A compound represented by formula (1)

$$R_{42}$$
 R_{42}
 R_{41}
 R_{11}
 R_{31}
 R_{21}
 R_{22}
 R_{23}
 R_{23}
 R_{23}
 R_{23}
 R_{23}

wherein

R₁₁, R₂₁, R₃₁, and R₄₁ independently represent a hydrogen or methyl group;

R₂₂, R₂₃, R₃₂, R₃₃, R₄₂, and R₄₃ independently represent any one of hydrogen, a linear alkyl group comprising 1 to 6 carbons, a linear alkyl group comprising 1 to 6 carbons to which a non-aromatic cyclic alkyl group or a substituted or unsubstituted aromatic ring is attached, a non-aromatic cyclic alkyl group, or a non-aromatic cyclic alkyl group to which a non-aromatic cyclic alkyl group or a substituted or unsubstituted aromatic ring is attached;

R₂₁ and R₂₂, R₂₂ and R₂₃, R₃₁ and R₃₂, R₃₂ and R₃₃, R₄₁ and R₄₂, and R₄₂ and R₄₃ may independently represent a non-cyclic structure without bonding to each other, or may independently represent a cyclic structure by bonding to each other through a linear alkylene group having a chain length of 1 to 5 carbons, a linear alkylene chain having a chain length of 1 to 5 carbons and carrying a branched chain of 1 to 6 carbon atoms, or a linear alkylene chain having a chain length of 1 to 5 carbons and carrying a cyclic structure of 1 to 6 carbon atoms; n can be selected from a range of numbers that enable the compound to have HDAC inhibitory activity; and

Applicant: Yoshida et al. Serial No.: 10/561,298 Filed: June 7, 2006

Page : 3 of 7

X represents a structural component having a structure that can coordinate with the zinc positioned at the active center of histone deacetylase.

2. (Original) The compound of claim 1, wherein X is any one of the substituents represented by the following structural formulas:

 OPD

Applicant: Yoshida et al. Attorney's Docket No.: 20214-0002US1

Serial No.: 10/561,298 Filed: June 7, 2006

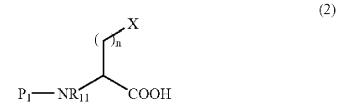
Page : 4 of 7

- 3. (Original) A histone deacetylase inhibitor comprising the compound of claim 1 as an active ingredient.
- 4. (Original) A tubulin deacetylase inhibitor comprising the compound of claim 1 as an active ingredient.
- 5. (Original) An apoptosis inducer comprising the compound of claim 1 as an active ingredient.
- 6. (Original) A differentiation inducer comprising the compound of claim 1 as an active ingredient.
- 7. (Original) An angiogenesis inhibitor comprising the compound of claim 1 as an active ingredient.
- 8. (Original) A cancer metastasis inhibitor comprising the compound of claim 1 as an active ingredient.

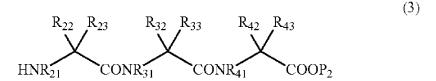
Attorney's Docket No.: 20214-0002US1

Applicant: Yoshida et al. Serial No.: 10/561,298 Filed: June 7, 2006 Page: 5 of 7

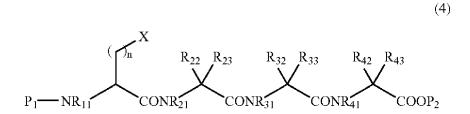
- 9. (Currently Amended) A pharmaceutical agent for treatment or prevention of a disease eaused by histone deacetylase, wherein the agent which comprises the compound of claim 1 as an active ingredient.
- 10. (Cancelled)
- 11. (Withdrawn) A method for producing the compound of claim 1, wherein the method comprises reacting a compound represented by formula (2)



(wherein n, R_{11} , and X are as defined in claims 1 and 2, and P_1 represents an amino protecting group) with a compound represented by formula (3)



(wherein R₁₁, R₂₁, R₂₂, R₂₃, R₃₁, R₃₂, R₃₃, R₄₁, R₄₂, and R₄₃ are as defined in formula (1) of claim 1, and P₂ represents a carboxyl protecting group) in the presence of a peptide coupling agent to yield a compound represented by formula (4)

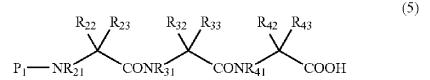


(wherein n, R₁₁, R₂₁, R₂₂, R₂₃, R₃₁, R₃₂, R₃₃, R₄₁, R₄₂, R₄₃, P₁, P₂, and X are defined above), then subjecting the compound represented by formula (4) to catalytic hydrogenation, acid treatment, or hydrolysis to remove P₁ and P₂, and subsequently, carrying out a cyclization reaction in the presence of a peptide coupling agent;

Applicant: Yoshida et al. Attorney's Docket No.: 20214-0002US1

Serial No.: 10/561,298
Filed: June 7, 2006
Page: 6 of 7

reacting a compound represented by formula (5)



(wherein R_{21} , R_{22} , R_{23} , R_{31} , R_{32} , R_{33} , R_{41} , R_{42} , R_{43} , and P_1 are as defined above) with a compound represented by formula (6)

$$\begin{array}{c} X \\ \text{HR}_{11}N \\ \end{array} \begin{array}{c} \text{COOP}_2 \end{array}$$

(wherein n, R_{11} , P_2 , and X are as defined above) in the presence of a peptide coupling agent to yield a compound represented by formula (7)

(wherein n, R₁₁, R₂₁, R₂₂, R₂₃, R₃₁, R₃₂, R₃₃, R₄₁, R₄₂, R₄₃, P₁, P₂, and X are as defined above), then subjecting the compound represented by formula (7) to catalytic hydrogenation, acid treatment, fluoride anion treatment, or hydrolysis to remove P₁ and P₂, and subsequently, carrying out a cyclization reaction in the presence of a peptide coupling agent; or

reacting a compound in which X of the cyclic tetrapeptide of formula (1) is a carboxyl group or a sulfhydryl group individually with trifluoroacetic anhydride, pentafluoropropanoic anhydride, or 1,1,1-trifluoro-3-bromoacetone to change substituent X into a different type of substituent.